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# ARCHIVES OF PEDIATRICS

A MONTHLY DEVOTED TO THE
DISEASES OF INFANTS AND CHILDREN
JOHN FITCH LANDON, M.D., Editor

## LEADING ARTICLES IN THIS NUMBER



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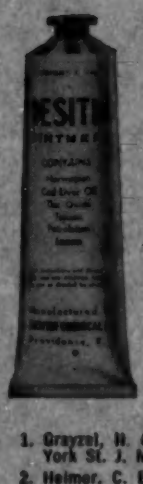

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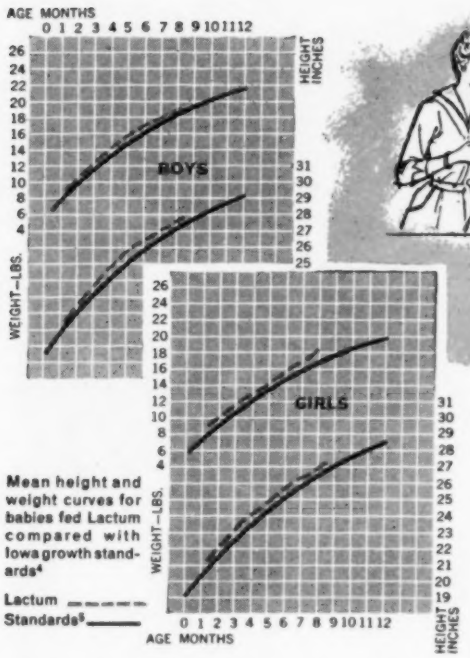


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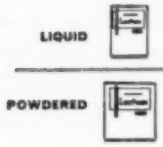


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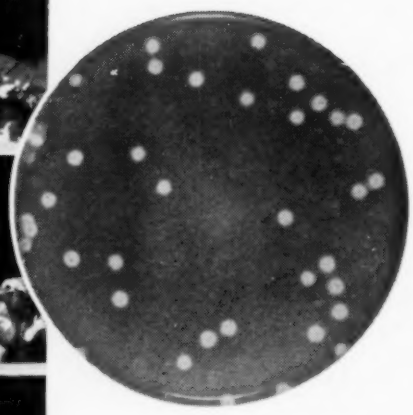

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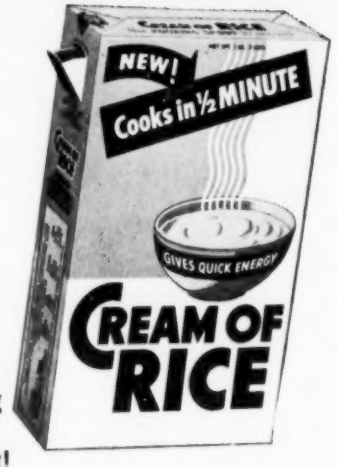


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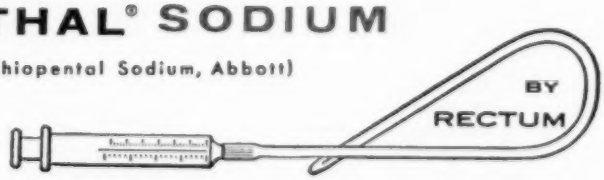


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# ARCHIVES OF PEDIATRICS

VOL. 71 JULY 1954 No. 7




## THE HYPERVENTILATION SYNDROME IN CHILDHOOD*

### REPORT OF TWO CASES


JAMES B. GILLESPIE, M.D.
Urbana, Ill.


Hyperventilation is of common occurrence in a clinical practice involving adult patients. In the usual instance it occurs as an acute, transitory episode characterized by gross hyperpnea and culminating in frank tetany. The strikingly acute forms of this syndrome are thus easily recognized. Attention has been called to the fact that when chronic patterns develop, various symptoms infrequently linked with the hyperventilation syndrome become increasingly prominent[1]. Under such circumstances, diagnosis may be more difficult.

Most often hyperventilation is of psychogenic origin and occurs in unstable persons who are tense, anxious or depressed[2]. Similar patterns, however, have been observed secondary to central nervous system disorders, such as encephalitis and drug encephalopathies[3, 4]. The experiences of terror, violent anger, severe pain, or other intense emotions may be productive of this type of dyspnea. It may occur during real anxiety and in episodes of anxiety neurosis. In certain situations, hyperventilation represents an hysterical conversion symptom, affecting the relief of an emotional tension. Hyperventilation occurs at high altitudes where the physiologic effects of anoxia provoke overbreathing through reflex mechanisms.


* From the Department of Pediatrics, Carle Memorial Hospital and Carle Hospital Clinic, Urbana, Illinois.

Respiration is controlled by both reflex and chemical mechanisms. The variations in respiration which occur during daily routine are caused chiefly by reflex phenomena. Afferent stimuli from any body organ, or on the basis of emotional alterations, may cause pulmonary ventilation to be increased beyond the level required by the metabolism of the body. This reflex increase in respirations furnishes the physiologic basis for many of the symptoms of the psychoneurotic patient. The patient may complain primarily of dyspnea or, rather, may complain of resultant symptoms, being unaware of the increased pulmonary ventilation.

The symptoms developed during hyperventilation are much the same regardless of etiology. They include numbness and tingling of the hands, feet and face; buzzing in the head; varying degrees of reduction in the level of consciousness, described as vertigo, faintness or light headedness; blurring of vision; dryness of mouth; and stiffness of the muscles and tetany. With reduction in the level of consciousness, anxiety, weeping and other hysterical reactions are common.

The sequential physiological changes responsible for the symptomatology have been outlined by Wiggers[5]. Reduction in alveolar $CO_2$ through hyperventilation causes acapnia, which is followed by alkalosis. These alterations in chemical environment seem to affect the metabolism of the cortex, as evidenced by alterations in the electroencephalogram, and the oxygen consumption of cerebral tissues is enhanced. Cerebral blood flow is reduced, owing to constriction of cerebral vessels, sometimes aided by lowering of systemic arterial pressure. The state of alkalosis produced may, under certain conditions, reduce the ionized calcium in the blood without necessarily affecting the total calcium. Such reduction in ionic calcium increases the excitability of peripheral sensory nerves, which manifests itself as numbness and tingling, and of motor nerves by producing various stages of tetany.

In addition to acceleration of the heart, other cardiac changes have been reported. The systolic discharge and minute output are said to decrease, and electrocardiographic changes suggestive of coronary insufficiency have been reported.

A correlation between reduction in consciousness and slowing of electroencephalographic frequency has been recorded[6]. The authors noted that high blood sugar, high oxygen tension, and

the recumbent position diminished electrocephalographic slowing. Intravenous injections of calcium chloride and nicotinic acid had no effect on the electrocephalogram during hyperventilation, and tetany was unrelated to the electrocephalogram and occurred with longer periods of hyperventilation. Actual syncope was unusual during hyperventilation.

In 1920, Grant and Goldman[7] produced convulsions by hyperventilation. Clinical seizures of the petit mal type may often be induced by deep breathing which need not be carried to the point of alkalosis[8]. Grand mal seizures are rarely produced by this means.

The relative frequency of the hyperventilation syndrome in women as compared to men has been commented upon by Schimmenti[9]. However, scant attention has been given to the occurrence of this syndrome in childhood, as judged by the absence of documented cases in the pediatric literature of the past ten years. Moreover the condition has not been mentioned or described in recent standard pediatric texts. It may be assumed, nevertheless, that the factors operating to produce such a syndrome in the adult may produce similar symptoms in children with personality dysfunction, as anxiety neurosis or hysteria. It would be anticipated that its occurrence will be more frequent in children at an age in which marked emotional disturbances are especially common. This would certainly include girls and boys within the pubertal and "teen" age ranges.

Two "teen"-aged girls, who have demonstrated the acute hyperventilation symptom complex on one or more occasions, have been observed. These two patients are reported because of the absence of similar reports of this syndrome in patients of the younger age groups in the pediatric literature.

## CASE REPORTS

*Case 1.* W. J., female, age 13 years, had always been in good general health except for repeated attacks of tonsillitis. Adenotonsillectomy had been performed in 1946. She had never menstruated.

On September 8, 1948 she complained of malaise, and the next day she was brought home from school because of severe headache and repeated emesis.

She appeared critically ill and was pale and disoriented when admitted to the Carle Memorial Hospital on September 9, 1948. The skin was cold and clammy, vomiting was recurrent, and she complained of numbness of the hands and feet. She was somnolent, poorly responsive, and respirations were shallow. A history of injury or poisoning could not be obtained.

The temperature was 35.5° C.; pulse, 130, and blood pressure 110/60. Physical examination, except for the findings previously noted, was non-informative. Neurological examination was negative. Hemogram disclosed the hemoglobin to be 13.8 grams: erythrocytes, 4,360,000; and leucocytes, 11,300 with 61 per cent neutrophiles, 37 per cent lymphocytes, and 2 per cent eosinophiles. Urinalysis was negative. Spinal fluid examination showed 1 lymphocyte per cmm.; protein, 29 mg. per 100 cc.; and sugar, 103 mg. per 100 cc. The fundi were normal, media clear, and extraocular movements and reflexes normal. Gynecological examination disclosed a normal juvenile pelvis.

An infusion of 5 per cent dextrose in saline was administered, and added heat was provided for the bed. Within three hours there was improvement with the temperature 37° C. and the pulse 90.

On September 10 she complained of headache and vertigo. Repeated leucocyte and differential counts were within the normal range. The diagnosis of hysteria was made and she was dismissed from the Hospital on September 11, 1948.

The patient remained in bed at home for several days and was then permitted up for short periods. On September 15, 1948, she was seen at home in an episode of clear-cut hysteria with crying, restlessness, headache, and complaint of numbness of the hands and feet. She was markedly hyperpneic, expressed fear of dying, and was quieted with sedation and reassurance. A diagnosis of hysteria with acute hyperventilation was made at that time.

Subsequently she suffered no further episodes of hysteria, hyperpnea, or other functional manifestations during a two-year period of observation.

*Case 2.* A. E., female, age 13 years, had been in good general health except for multiple exostoses which were symptomless. She was a high-strung, tense, hyperactive, irritable girl with parents who were also tense and emotional.

On February 5, 1952 she complained of headache, nausea and malaise. Vomiting with mild diarrhea occurred on February 6. On examination that day she did not appear acutely ill. The temperature was 36° C., marked hyperpnea was present, and both hands were held in the carpopedal position. The pharynx was mildly injected, and the odor of acetone was apparent on her breath. A hemogram was within the normal range. She was given an infusion of 5 per cent dextrose in saline, intravenous calcium gluconate, and parenteral penicillin. Diagnosis on this occasion was a "grippal" infection with vomiting and resultant alkalosis.

There was no recurrences until June 1952, when she attended a summer camp for girls. On June 22 she suffered mild otitis media. A week later, following attendance at a movie, vertigo, headache, hyperpnea and complaint of faintness occurred. The hands assumed the carpopedal position, and the legs and arms were stiff. Sedation was prescribed by the camp physician, and symptoms subsided within eight hours. Three identical episodes occurred within the subsequent week, and she was brought home from camp.

On examination July 28 weight was 101 pounds and height 61 inches. The blood pressure was 126/80, and the vision was 20/30 in the left eye and 20/50 in the right eye. Physical examination, otherwise, was non-informative. The hemogram and urinalysis were within normal limits. The serum calcium was 10.6 mg. per 100 cc. and the serum phosphorus was 3.7 mg. per 100 cc. X-ray of the skull was negative. The consulting ophthalmologist found the fundi normal and noted the reduction in visual acuity; in his opinion the headaches were not on an ocular basis. The diagnosis of hyperventilation syndrome with multiple trigger mechanisms was made.

Vomiting from both psychogenic and organic causes and perhaps migraine, were productive of the hyperventilation syndrome in this patient. Phenobarbital several times daily was prescribed for two months, and Cafergot was advised in event of a migraine episode. There were no recurrences of these episodes in the subsequent eighteen months and she continued to lead a very normal life.

## COMMENT

Both of the reported female patients were high strung, emotionally unstable, hyperactive and tense. The first patient had suffered considerable emotional upset occasioned by the death of her father. At the time of her illness the mother was contemplating remarriage and had discussed this with the children. The family resources were limited, and inability to dress and do as her school classmates had been a source of aggravation to the patient.

The second child was a member of a family in which both parents had been divorced and remarried. The parents of this patient were particularly tense and emotional, and she and her father were in frequent conflict.

In both girls the episodes, while recurrent, were of an acute type and did not become chronic. For many months neither girl has had complaints of a functional nature.

Treatment of the hyperventilation syndrome depends largely on the diagnosis which enables the physician to offer an explanation of the condition to the patient and the family. By avoiding the practice of forced breathing, by temporarily holding the breath, or by rebreathing air exhaled into a paper sack, the patient may bring about alleviation of symptoms within a few minutes. By means of these measures carbon dioxide is allowed to reaccumulate in the alveolar air.

It is probable that hyperventilation syndrome in children is not as rare as the absence of reports in the literature would indicate. Attention is called to the occasional occurrence of this symptom complex in patients of pediatric age, since such children may have bizarre complaints and the exact diagnosis may be in doubt unless the occurrence of hyperventilation syndrome is borne in mind.

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# FIEDLER'S MYOCARDITIS*

## Review of the Literature with Report of a Case

A. El Gholmy, M.B.; S. Aidaros, M.D.;
M. El Nabawy, M.D. and Mamdouh Gabr, M.D.
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Fiedler, in 1899[1], described five cases in adults who showed an isolated form of acute interstitial inflammation of the myocardium. Since then, several cases were described in the literature, especially in Germany. Few cases, however, were described from other countries until 1929 when Scott and Saphir[2] drew attention to that disease in the U.S.A. Several cases of the disease in young adults were described from various countries since that time under different names: isolated myocarditis, interstitial myocarditis, acute myocarditis, subacute myocarditis, fibrinous myocarditis, productive myocarditis, etc.[3]. The disease, however, seems to be rare in infancy and childhood. Conlin and Mantz[4], in 1953, found only 26 cases in infants below 22 months. The first case in a child was reported by Zuppinger[5], in 1901. Several cases were later described in that age period[6-13]. There is little data as to the incidence of the disease in infancy and childhood. Saphir[14] found three cases of Fiedler's myocarditis in a series of 97 autopsies of myocarditis from various causes in childhood, excluding infectious diseases.

The pathological changes in Fiedler's myocarditis are not specific in the anatomic sense[13, 15]. Classically defined, Fiedler's myocarditis is an isolated involvement of the myocardium by a diffuse non-specific inflammatory process without involvement of the endo- or pericardium[13]. The disease, as first described by Fiedler is an interstitial inflammation. He did not describe parenchymatous changes in the myocardium, but Schmorl, who studied Fiedler's cases microscopically, found definite parenchymatous changes in some of the hearts. Actual muscle fibre degeneration and fragmentation was later reported in some cases[15, 16], but extensive necrosis of the muscle fibres was not reported[17]. The type of cellular infiltration present is mainly lymphocytic, but plasma cells, histiocytes, mononuclears and polymorphs may also be encountered[13, 15]. Even cases with eosinophilic infiltration were described[13]. Everly

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and Marshal, however, consider it safer to restrict the term Fiedler's myocarditis to those cases where the inflammation is mainly lymphocytic[16]. A perivascular distribution of the inflammatory cells is sometimes conspicuous, but these perivascular accumulations never resemble rheumatic myocarditis[13]. The degree of cellular infiltration varies, sometimes only small foci of subacute inflammation being present[4, 13, 18]. A granulomatous form of Fiedler's myocarditis was described by Saphir[19], in 1941, and he states that if syphilis and tuberculosis could be excluded in such granulomatous forms they should be considered examples of Fiedler's myocardits was described by Saphir[19], in 1941, and similar collagen diseases should be excluded in such granulomatous forms and the term Fiedler's myocarditis should be better restricted to the diffuse infiltrative form[16]. Boikan[20], in 1931, described a chronic type of the disease with evidence of healing in the heart, but Everly and Marshal state that "a reparative process is absent in Fiedler's myocarditis." The endocardium was not affected in all reported cases. Endocardial thickening may sometimes be present[15, 16]. This endocardial thickening is common as a secondary response to anoxia in many cases of myocarditis[21]. The cases that were described with marked endocardial fibrosis were actually examples of endocardial fibroelastosis[15, 22]. This confusion is due to the fact that occasional myocardial changes may be present in endocardial fibroelastosis secondary to the endocardial lesion[23]. All cardiac chambers may be affected in Fiedler's myocarditis. The left side of the heart, the left ventricle in particular, is usually more affected by the infiltration than the right side[13].

The disease is commonest in young adults, but apparently any age may be affected. Cases were described in newly born infants[24], and many cases of so-called congenital idiopathic hypertrophy of the heart are examples of Fiedler's myocarditis[16]. It is classically described to give rise to a picture of acute congestive cardiac failure with a rapidly progressive course terminating fatally in a few weeks time. Sudden death is common, and the possibility of Fiedler's myocarditis should be considered in any case of sudden death in the young[14]. Other cases were described to run a protracted course; one of Fiedler's original five cases lived for a long time[1] and proved cases were reported with a history of several years duration[10, 15, 16, 21, 25].

Clinically, a low grade fever is commonly present[16]. The heart is enlarged with tachycardia, gallop rhythm, and no significant murmurs, evidence of congestive heart failure, viz., dyspnoea, cyanosis, oedema of lower limbs, congested neck veins and congested liver are present to a variable extent. Chest pain may be complained of in adults. Cardiac thrombi and embolic phenomena are common in the lungs and peripheral vessels[26]. Cardiac arrythmias are not rarely associated with the disease, especially in infants. Three cases of paroxysmal tachycardia in infants proved at autopsy to be cases of isolated myocarditis[24].

Investigations are of little value in the diagnosis. X-ray shows a generalized enlargement of the cardiac silhouette, and electrocardiographic changes of myocardial strain are present. A prolonged conduction time and cardiac arrythmias may be encountered[13]. The blood count and sedimentation rate are usually within normal limits.

The clinical diagnosis of Fiedler's myocarditis is usually made by exclusion[26]. All causes of myocarditis should be excluded before the diagnosis of isolated myocarditis is ventured. Common causes of cardiac disease are easily ruled out; thus myocardial diseases secondary to infectious toxins, nutritional disorders or other systemic diseases are easily diagnosed by the presence of the primary cause.

Congenital heart disease rarely is present without murmurs and even then angiography and cardiac catheterisation settle the diagnosis. Rheumatic carditis is almost always associated with clinical evidence of valvulitis as well as definite rheumatic history. Cases of rheumatism in infancy may be a real difficulty, due to the bizarre form of rheumatism at that age[27]. There are instances on record of rheumatic myocarditis without endocardial or valvular involvement[13]. The diagnosis in such cases may be settled only at autopsy. Many of the reported cases of Fiedler's myocarditis were clinically diagnosed as pericardial effusion[14, 28]. This difficulty arises due to the low pulse pressure, pulsus paradoxus, distant heart sounds, as well as the radiological and electrocardio graphic changes. Pericardial tapping is of course diagnostic. Rare forms of primary myocardial disease in young infants, viz., glycogen storage disease, aberrant left coronary artery and medial necrosis of the coronaries usually manifest themselves before the first six

months of life and they are rarely associated with evidence of congestive cardiac failure[21]. The rare forms of endocardial fibroelastosis not associated with cardiac murmurs may be impossible to diagnose from Fiedler's myocarditis before autopsy. Rosenbaum, however, states that the diagnosis of Fiedler's myocarditis in such cases should be entertained if the infant is beyond six months of age, with evidence of congestive heart failure, abnormal heart sounds and a good response of the congestive failure to digitalis therapy[21].

The difficulty in diagnosis of Fiedler's myocarditis does not only face the clinician but may also be present at the time of autopsy[13]. It may sometimes be necessary to examine numerous sections from various blocks of the heart before the diagnosis is made[4, 13]. It is important to make a complete autopsy of all organs with careful microscopic examination in order to exclude pathologically all possible causes of myocarditis before diagnosing isolated myocarditis. Many rare diseases, such as trichinellosis and blastomycosis, should be carefully looked for[14].

Many etiological factors were held to be responsible for the disease. Probably cases of Fiedler's myocarditits may be of varied etiology with a common pathological picture[13, 29]. Fiedler's myocarditis was at one time thought to be the cause of sudden death in status thymolymphaticus and several reported cases were associated with enlargement of the thymus[11, 19]. This was not, however, later confirmed. An allergic origin of the carditis is still considered by many authors to be present. A common association of eczema was reported by several authors[14]. Allergy to drugs, especially sulphonamides, is said to produce similar myocardial changes[31]. A virus infection of the myocardium was also suggested as a possibility. Fiedler himself, in his original description of the disease, suggested that a microparasite may be responsible for the condition[1]. Helwig and Schmidt[32], in 1945, isolated a virus from anthropoid apes dying of interstitial myocarditis. No evidence of such virus infection, however, was present in the reported cases. Saphir[19], in 1941, drew attention to the common association of upper respiratory infection in cases of Fiedler's myocarditis. This was also noticed by other authors[4], but the definite relationship between these two conditions is unknown. Nutritional disturbances were also suggested as etiological factors. Myocarditis, similar to

those present in beriberi, were occasionally described in a few cases[4, 13], but no evidence of vitamin deficiency was present in these cases. Deficiency of potassium was lately reported to produce a myocarditis in rats[33], but potassium deficiency was never reported in isolated myocarditis. It is safer at the present time to consider that the etiology of Fiedler's myocarditis remains unknown.

Due to paucity of reported cases of Fiedler's myocarditis in infants, the following case report may be of interest.

## CASE REPORT

H.G., a boy, aged 20 months, was admitted to hospital on March 12, 1953 with the complaint of dyspnea, severe cough, slight cyanosis and vomiting for the last two months. The symptoms were gradually progressive, with loss of weight and appetite.

The patient was a breast-fed baby, born at full term after an uneventful pregancy. He developed normally and had no special infectious diseases or other maladies during his first 18 months of life. There was no family history of significance.

Examination revealed: a moderately built infant, weighing 9½ kilos, markedly dyspneic, respiratory rate 65 per minute with marked contraction of accessory respiratory muscles. There was a subcyanotic tinge of the lips and a puffy face. There was no clubbing of the fingers. The feet were slightly edematous. A low grade fever was present. Pulse 128 per minute; blood pressure 100/65. Neck veins were full and slightly pulsating. Heart: apex in the sixth space anterior axillary line, diffuse but not well seen. There was dullness for 1½ inches in the second left intercostal space. The heart sounds were faint and a gallop rhythm was heard just inside the apex. No murmurs were audible. Pericardium was tapped and a few centimeters of clear fluid could be aspirated and proved to be a transudate.

Examination of the chest revealed a few fine non-consonating crepitations over both bases.

The liver was enlarged three fingers under the costal margin, firm and very tender. No ascites was present. There was no palpable spleen, and the thymus and lymph glands were normal.

The nervous system was free and knee jerks were present.

*Investigations.* The blood showed moderate anemia: Hemoglobin, 55 per cent; R.B.C., 2,500,000; W.B.C., 10,000; polys,

49 per cent; lymphs, 44 per cent; monos, 5 per cent; eosins 2 per cent; erythrocyte sedimentation rate, 10 mm. per hour.

Urine was normal apart from a faint trace of albumin. Stools were free.

Tuberculin reaction: negative. Stomach wash for T.B.: negative. Cold agglutinins: negative. Blood urea: 30 mgm. %

Electrocardiogram: left ventricular strain pattern in a vertical heart, hypertrophied.

X-ray: Huge diffuse enlargement of the cardiac shadow. The cardiac borders were ill-defined; the radiological picture suggested myocardial lesion of the heart, with flabbiness of the cardiac muscle. There was enlargement of both ventricles in the left oblique view. There was no enlargement of the left auricle in the right oblique view, the whole oesophagus being displaced backwards by the enlarged heart (Figs. 1 and 2).

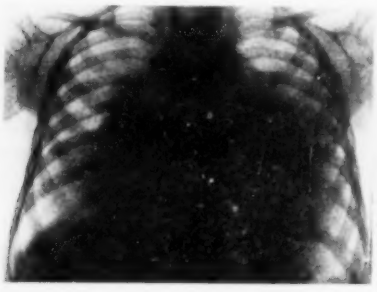


Fig. 1. Anteroposterior radiogram showing flabby enlarged heart.

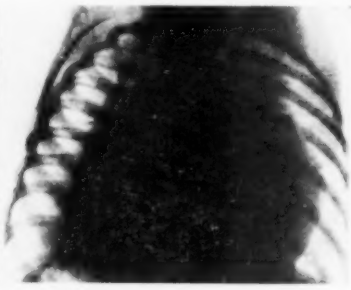


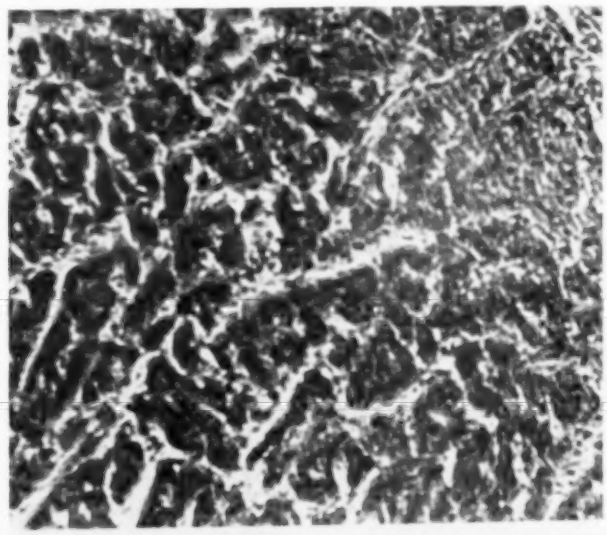
Fig. 2. Left oblique radiogram showing enlargement of both ventricles.

Screening revealed slight pulsations of the heart, hilar congestion but no hilar dance.

Progress: The clinical manifestations of cardiac failure progressed in spite of medical treatment by digitalis and antibiotics. The patient died on April 11, 1953 and autopsy was carried out.

*Autopsy.* The heart was definitely enlarged, weight 130 gm. (normal for that age 48 gm.). The left ventricle was hypertrophied and dilated; its wall was 6 mms. thick. The right ventricle was also hypertrophied and dilated to a less extent; its wall was 3 mms thick. The myocardium of both ventricles showed some toxic degeneration. The endocardium was opaque, especially in the left

auricle. The valves were all normal and shiny. The pericardial sac contained less than 10 cc. of clear fluid; the two layers were smooth



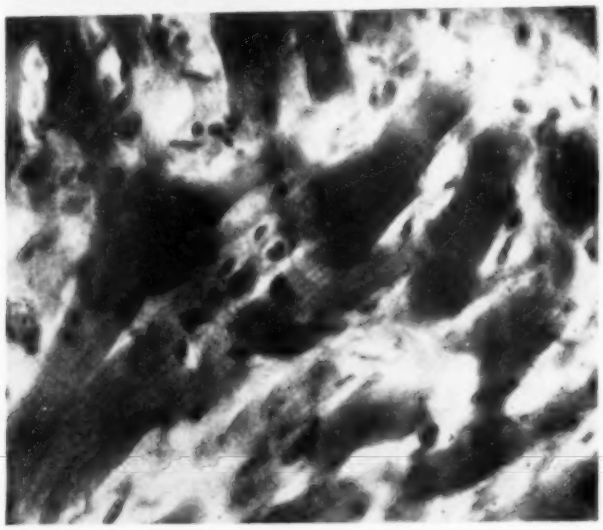


Fig. 3. (Top) Low power (X 100). Cellular infiltration under pericardium and in between muscle fibers.

Fig. 4. (Bottom) High power (X 330). Lymphocytic infiltration between muscle fibers.

and shining. There was only a small hemorrhagic spot, traumatic in origin, from the aspiration needle. No congentital abnormalities were present and the coronary arteries were normal.

*Microscopically.* The interstitial tissue of the ventricular and auricular myocardium showed dilatation and injection of the blood vessels. There was peri- and paravascular cellular infiltration which was seen localized and diffuse in various blocks cut from the four chambers of the heart but mainly affecting the left ventricle. This cellular reaction was also extending under the pericardium and in between the muscle fibres in various proportions. The cells were mainly lymphocytes and to a slight extent small histiocytes. There was a notable absence of polymorphs and Achoff's cells (Figs. 3 and 4). Few foci of early necrosis were also visible in some blocks together with some early fibroblastic reaction, but there was no evidence of any marked fibrosis. The endocardium showed no excessive deposition of any collagenous or elastic tissue as proved by van Gieson stain. There were no microscopic abnormalities in the valves, coronaries or pericardium.

The lungs, spleen, intestines and kidneys were all the seat of chronic venous congestion.

The lungs showed numerous hemorrhagic infarcts of various shapes and sizes, but there was no evidence of bronchopneumonia, fibrosis or any changes in the pulmonary vasculature.

The liver presented the appearance of a nutmeg liver besides an early microscopic picture of mono- and multilobular cirrhosis which was most probably dietetic in origin. There was no evidence of bilharziasis.

All other organs, including endocrines and thymus, were found normal and showed no congenital abnormalities.

## COMMENTS

Although several cases of Fiedler's myocarditis in infants were reported from Germany and U.S.A., very little interest in that disease was present in other countries. The first case of Fiedler's myocarditis in an infant was described in England in 1948[16]. The above reported case is the first case of Fiedler's myocarditits reported from Egypt.

The reported case was presented clinically as a case of heart failure of unknown etiology. There was no history or clinical evidence

of infection or disease that could secondarily affect the myocardium with resultant failure. The sudden onset at one and a half years and the absence of clinical evidence of congenital heart disease ruled out that condition as a cause. The age, the absence of rheumatic history, the absence of murmurs, as well as the absence of any other rheumatic manifestations, were strong evidences against the diagnoisis of rheumatic carditis. It was, however, difficult to rule out that possibility altogether before death. Rare forms of primary myocardial disease in infancy, such as glycogen storage disease, aberrant coronary artery, congenital hypertrophy of the heart, medial necrosis of the coronary arteries, were excluded by the age of onset of the disease as well as the absence of characteristic electrocardiogram changes. In spite of the absence of murmurs, the possibility of endocardial fibroelastosis could not be absolutely eliminated on clinical grounds. Few cases without murmurs were recently described[21]. The left ventricular preponderance present in our case is a common feature in that disease. Fiedler's myocarditis, however, was felt to be the most tenable clinical diagnosis.

Autopsy confirmed the diagnosis of Fiedler's myocarditis in that case. The typical features of that disease were present:

1. An absence of endocardial or pericardial involvement. The slight thickening of the endocardium of the left auricle was reported to occur in many cases of Fiedler's myocarditis[15, 16].

2. There was no extra cardiac lesion, pulmonary, renal, endocrine or otherwise, that could account for the cardiac condition.

3. The typical myocardial changes of Fiedler's myocarditis were all present in this case: A diffuse cellular infiltration mainly lymphocytic in the interstitial tissue and in between the muscle fibres. Few foci of degeneration of the muscle fibres were present and there was a slight fibroblastic reaction in some areas but no gross fibrosis. The absence of any polymorphic infiltration in our case was characteristic. There was also a definite perivascular and subpericardial collection of the infiltrating cells. This was reported by several authors. The brunt of the lesion in our case affected the left ventricle. This was usual in most of the reported cases[13, 15].

Rheumatic myocarditis was definitely excluded in this case, due to the absence of any endothelial reaction as well as the different type of cellular infiltration present.

No evidence of subendocardial sclerosis (endocardial fibroelastosis) was present. The fibroelastic tissue of the endocardium was normal.

The multiple pulmonary infarctions were characteristic in the reported case. They are most probably secondary to cardiac thrombi which commonly occur in Fiedler's myocarditis[26].

No conclusion as to the etiological factor in the reported case could be made out. The early dietetic cirrhosis of the liver is apparently an associated feature. Saphir stated that it cannot be related to the cardiac condition[14].

## SUMMARY

The literature on Fiedler's myocarditis is reviewed with special reference to the disease in infants and children.

A case of Fiedler's myocarditis in an infant 20 months old, verified by autopsy, is reported. The importance of Fiedler's myocarditis as a cause of obscure heart failure in the young is stressed.

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# THE DIAGNOSIS AND TREATMENT OF MENINGITIS IN CHILDREN*

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Most of the acute infectious diseases have made a phenomenal decline[1, 2] in prevalence during comparatively recent times. But the incidence of meningitis seems to vary much the same as it has in the past. In respect to meningococcic infections this is not strange because there is no method for active immunization and the source of infection is seldom known. Furthermore, neither race, state of nutrition or sanitary conditions appear to be an important influence in resistance to meningococcic meningitis in children.

The term "primary meningitis" frequently has been used when the manner of infection was undetermined. But meningitis may be properly regarded as a complication of a systemic disease or as a result of direct extension from some focus, as the ear or facial sinuses. In many instances of purulent meningitis[3] it is possible to obtain a positive blood culture at the onset of the disease. However, it is not so simple to make a precise diagnosis if the etiologic factor is a virus, spirillum, fungus or some other uncommon organism. Moreover, an aseptic meningitis may cause confusion. Tetanus and also meningismus may be mistaken for meningitis.

In contrast to some of the common contagious diseases, meningitis may be witnessed at any time after birth. When there is such an occurrence in a child who is less than a week old, it is advisable to think of B. coli as the offender. Nevertheless, staphyloccus aureus[4] meningitis has been reported in a three-day infant and salmonella and pyocyaneous infections, during the first weeks of life.

The signs and symptoms of meningitis in early infancy are not always the same as in children of more advanced years. Occasionally, there is no neurological evidence to suggest the presence of meningeal irritation. There may not be bulging or even tenseness over the anterior fontanel. However, there is a septic type of temperature which may range from 99° to 103° F. daily and yet a physical examination fails to explain the cause of the illness and

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perhaps the refusal to take nourishment. Under such circumstances it is well to remember that the examination is not complete without a lumbar puncture. When that is done it may be found there is a purulent cerebrospinal fluid which contains H. influenzae.

Hemophilus influenzae infection has one particularly unusual characteristic among the more common meningitides. It seems to single out the very young for attack and is seldom witnessed in adults. It has been estimated that 90 per cent of the cases occur among those who are 5 years of age or less. Therefore age may be a factor in forecasting or excluding the kind of meningitis that a patient has.

The onset of influenzal meningitis is usually very abrupt, with a temperature which may rise to 105° F. or more. At the same time there is occasionally a circumstance which is not likely to be observed in any other form of meningitis. The child develops a sudden edema about the glottis and, with neurological signs lacking, a diagnosis of laryngeal diphtheria is sometimes made. At this stage of the disease a blood culture is almost certain to disclose the influenzal bacillus. But, if the patient survives the respiratory threat against his life, stiffness of the neck and all the customary signs of meningitis become evident within the following 12 hours. Death is almost certain to intervene if a prompt tracheotomy is not performed. However, in the average case of H. influenzal meningitis, the abrupt onset with high fever is accompanied by deep stupor or coma and in infants there will be no tenseness or perhaps bulging over the anterior fontanel. The picture presented is similar to that of tuberculous meningitis with which the diagnosis is sometimes confused.

With influenzal meningitis there are no petachiae, as a rule, to aid in a clinical diagnosis so a lumbar puncture is required for examination of the cerebrospinal fluid. The cell count generally is not as high as with most forms of acute purulent meningitis. Nevertheless, occasionally the polymorphonuclears approximate 5,000. Organisms may be difficult to demonstrate on a stained smear, but a culture of the spinal fluid should supply the desired proof. Rarely, when the spinal fluid is examined early in the attack, lymphocytes are found to predominate and a mistaken diagnosis of nonparalytic poliomyelitis is made.

Although tuberculous meningitis may occur at any age, it is

encountered most frequently in children. But cases before one year have not often been observed among our hospital patients. With this disease the onset is more likely to be gradual rather than abrupt, as in most kinds of meningitis. For that reason the nature of the illness is not always recognized before the meninges are seriously involved. In the beginning, headache is the most constant complaint by those who are able to give an expression of their distress. Vomiting is also a common symptom and loss of weight may be noticeable before stiffness of the neck is disturbing to the patient or detected by a physician. In the meantime there will be a daily elevation and remission of temperature which may not rise above 103° F.

With one exception, the cerebrospinal fluid of the tuberculous meningitis patient may resemble quite closely the cerebrospinal fluid of poliomyelitis. In each instance the spinal fluid is clear or has a ground glass appearance. Cell counts usually do not range beyond the hundreds and lymphocytes largely predominate as a rule. However, with either disease, polymorphonuclears may be supreme early. But the spinal fluid glucose is diminished and often lower in tuberculous cases than in any other form of meningitis, whereas in poliomyelitis the glucose is normal or even elevated. Nevertheless, confusion occurs in a differential diagnosis of these diseases, especially during the poliomyelitis season. This may be attributed partly to the fact that the tubercle bacillus is not detected on smear in more than 50 per cent of spinal fluids in tuberculous meningitis.

If tuberculous meningitis is considered as a possible diagnosis, an x-ray of the chest may disclose a responsible focus. If the patient is an infant or young child, a Mantoux test is sometimes helpful in making a decision. It may also be advisable to obtain stomach washings. But in every instance a guinea pig inoculation should be made.

There is one sign which has always impressed the writer as significant in making a clinical diagnosis. Inequality of pupils is fairly frequent with tuberculous meningitis during the early stage. It seems to be present more often in infants and young children than with older patients. Inequality of pupils is very rarely present with other forms of meningitis. If it occurs late, a brain abscess may be suspected. Some form of paresis or paralysis occurs more

frequently with tuberculous infections than with other kinds of meningitis. If tubercle bacilli are not readily found in the spinal fluid, it is well to make both a Levinson and a tryptophane test. A brain tumor or brain abscess may be a cause for uncertainty in diagnosis.

Pneumococcic meningitis is also fairly common among the meningitides. And often it is witnessed independently of any lung infection. Whenever a meningitis patient has a history of a skull fracture, regardless of the time that may have elapsed since the injury, it is advisable to consider the pneumococcus as the most probable cause of the meningeal infection. This has been found to be true repeatedly in our hospital patients. Nevertheless, it is usually believed that the ear is most frequently the focus of infection. There is nothing which can be said about the appearance of the patient that is characteristic. But recurrences or second attacks are more common than with other forms of meningitis. This applies to children as well as to older persons. An etiologic diagnosis must be made by finding the organisms in the cerebrospinal fluid. A blood culture early in the attack may also reveal pneumococci.

From many standpoints meningococcic infections are the most important. First, they are, as a rule, the only ones associated with meningitis which are designated as contagious. A second point is that meningococci generally account for more cases of meningitis than any other organisms. Moreover, the disease can be endemic, sporadic or epidemic.[5] And in the last event the carrier rate in a community has been estimated to be as high as 36 per cent of the population. Thirdly, this is the only form of meningitis that is likely to have petechiae in the skin and mucous membranes. Fourth, if petechiae[6] are present, a smear from one of the lesions often will demonstrate the organism. Under the latter conditions a lumbar puncture is not a necessity for a bacterial diagnosis. Also early in the course of the disease, especially if petechiae are present, a blood culture is frequently positive. A fifth point of special interest is that meningococci account for nearly all examples of the Waterhouse-Friderichsen syndrome.

Based on the notations enumerated, it seems apparent that a prompt diagnosis is particularly urgent in cases of meningococcic infections if transmission of the disease is to be prevented. Further-

more, if petechiae are observed an accurate diagnosis should be much easier to make than in other forms of meningitis. But because a patient does have petechiae, either with a meningococcemia alone or an accompanying meningitis, a number of errors occur. Meningococcic infections have been mistaken[7] for measles, chickenpox, smallpox, typhoid, typhus, subacute bacterial endocarditis, leukemia and various forms of purpura, as well as drug eruptions.

Patients with the Waterhouse-Friderichsen syndrome may be in such profound shock that they die within a few hours and may not have been seen by a physician. Many times in the case of that syndrome the cerebrospinal fluid is clear and laboratory examination negative.

Among the less common forms of meningitis in children not alluded to in the beginning of this discussion, pseudomonas aeruginosa (pyocyaneus), Friedlander's bacillus, streptococcus and very rarely trichinae are the organisms responsible for the condition. In case of the last named, unusual tenderness of muscles and puffiness about the eyes may suggest the possibility of trichinosis. Generally, without great difficulty, trichinae will be found in the cerebrospinal fluid. Also an eosinophilia should be expected. As a rule, among the infrequent kinds of meningitis, there are no characteristic signs which are likely to be an aid in forecasting an etiologic diagnosis. Therefore, a lumbar puncture and examination of cerebrospinal fluid is necessary. Previously, the ears were referred to where there is clinical evidence suggestive of meningitis. Their examination as possible foci of infection should not be neglected. We scarcely ever see a meningitis patient with a suppurative otitis media unless the ear is the focal point for the meningeal infection. This observation suggests that a culture from the aural canal may determine the nature of the organism that has invaded the meninges. As formerly indicated, the pneumococcus then is perhaps the first organism on which suspicion should be cast but streptococci may account for the condition. The organism may be identified on a smear, but a spinal fluid culture should be positive for confirmation.

I have cited certain signs and symptoms which seem to be characteristic for several different kinds of meningitis. However, there are findings which are more or less common for all forms. In most instances the onset is abrupt. Even with tuberculous menin-

gitis such a history is occasionally given. Convulsions are always associated with infants and young children at the beginning of the illness. But after admission to hospital scarcely 10 per cent of the patients have convlusions. Aside from tuberculous patients, vomiting is not a common occurrence. Elevation of temperature is always to be expected. It may gain a height of 105° to 106° F. before treatment is instituted. The patient may be comatose, wildly delirious, irrational or clear mentally. Stiffness of the neck is the most constant sign but may be absent in infants, as previously mentioned. The Kernig and Brudzinski signs are nearly always present. Reflexes may be exaggerated early in attack and absent later. Strabismus is not rare early in any form of meningitis and may persist for a number of days.

When an etiologic diagnosis of meningitis is to be made, the two commonest forms, namely meningococcic and tuberculous, should be given first consideration. The presence of petechiae in the skin, and perhaps also in the conjunctivae, is usually sufficient to exclude the tuberculous. An x-ray film indicative of pulmonary tuberculosis nearly always points to the organism concerned with an existing meningitis.

One might feel that a great deal of time and thought are expended by undertaking to make a clinical diagnosis that will be confirmed by the laboratory. Sometimes the physician's attitude is "have a lumbar puncture made and find out what the laboratory says." And that might be a simple procedure in the hospital, but we do not believe it is a proper plan to advocate when teaching medical students. Furthermore, the physician who may be obliged to care for a patient at home is not likely to have a laboratory and a technician close at hand. In addition, the patient's family may wish to know what kind of meningitis you propose to treat. Is it contagious? If so, what will you do to protect the family? Is the patient going to die or will he be a mental defective in case of survival? Some of these questions will be more readily answered if you have made a critical inspection of the patient.

In my own city there are doctors who have a very large practice yet may seldom see a meningitis patient. Under such conditions it is not strange that an error in diagnosis can occur. Therefore, it is advisable to study carefully each meningitis patient and attempt to make a tentative diagnosis that will be upheld by the laboratory.

Ordinarily isolation regulations are required only for meningococcic patients. However, some of our states also classify tuberculous meningitis as a communicable disease. If the patient has an open case of tuberculosis, justification for that action is apparent. The mere fact then that a meningitis patient may have a communicable disease emphasizes the importance of a prompt diagnosis.

Our plan of treatment for all forms of meningitis is much the same. There is no intrathecal therapy[8] and more than one spinal tap is rarely made. The chief variations in therapy are based on the selection of the remedy considered most appropriate. Usually it is not necessary to conduct a series of sensitivity tests before beginning treatment because generally the results of scientific investigations have demonstrated the effectiveness of several sulfonamides and antibiotics which are capable of bringing about recovery of the patient concerned. Nevertheless, if there does not seem to be the proper response to the remedy being used, then sensitivity tests should be conducted.

For meningococcic infections, antimeningococcus serum or meningococcus antitoxin[9] is not likely to be obtainable even if the physician desired to use it. But almost any of the sulfonamides can be prescribed, including sulfathiazol,[10] if there is a preference for a sulfa drug. Before development of the antibiotics we had excellent results with either sulfadiazine or sulfathiazole, although an inscription on the package of the latter said "do not use for meningitis." The warning was issued because sulfathiazole did not readily pass into the cerebrospinal fluid but its accomplishments were of a superior order. Hematuria was a frequent occurrence with the sulfa drugs and, even on rare occasions, blocking of ureters with crystals was reported. At present the sulfonamides are seldom used in our contagious disease hospital because we believe the antibiotics are preferable.

Penicillin, aureomycin or terramycin[11] are the antibiotics most likely to be thought of in connection with meningococcic meningitis. Some physicians still administer penicillin intrathecally as well as by other routes and perhaps for that reason give it preference. However, penicillin, intraspinally, is a procedure which can lead to disastrous results.[12] But if penicillin is favored it must be given in massive doses, perhaps several million units daily to bring about

recovery. With penicillin a sulfonamide is often selected because of a synergism believed to exist when these remedies are given in combination.

Aureomycin or terramycin is particularly effective against the meningococcus. These drugs may be prescribed intravenously or orally under suitable conditions. For infants and young children, oral administration of medication is not always satisfactory. The child may resist treatment and a portion of the dose may be lost, or the patient unobserved may expectorate the dose of medicine which has been held in the mouth. Sometimes infants regurgitate or vomit shortly after medication has been swallowed. In any such instance the beneficial effects of the remedy are mitigated or destroyed. Chiefly, on account of those reasons, oral medication for seriously ill infants or children is ill advised if other methods can be adopted.

As a rule our patients are given the initial dose of the chosen remedy intravenously.[13] If necessary a cut-down is made on a suitable vein to introduce the needle, generally, on the dorsum of the foot or perhaps on the forearm or back of the hand. If the dilution is 1 cc. or more of 5 per cent dextrose to each milligram of the drug there is not likely to be any difficulty in regard to thrombosis. Nevertheless, it is a good precaution to discontinue medication by vein as soon as possible if another route is satisfactory. Because some of the antibiotics can be injected in the muscle, a change in method of administration may be a simple matter. However, the oral route is satisfactory only if it is known the drug is retained. It should not be given on an empty stomach.

Dosage of the antibiotic is commonly based on body weight and a scale of 50 milligrams of the drug per kilogram often used. However, we usually pay more attention to the severity of the disease and the age of the patient. An infant may receive as little as 125 milligrams of aureomycin or terramycin for the initial dose but in most instances it will be double that amount. Thereafter the dosage may be decreased or continued unchanged, depending on the condition of the patient, and prescribed at 6-hour intervals. Duration of medication ranges from 6 to 10 days for most patients. It is discontinued when temperature has remained normal for 48 hours.

Although it is not unusual for physicians to prescribe a sulfona-

mide as well as several antibiotics for the treatment of meningitis, a single remedy is generally sufficient. And with a multiplicity of drugs the possibility of antagonistic action may require consideration. Sedatives are very seldom required for meningitis patients. Morphine should never be used, as it depresses respiration and tends to increase edema of the brain. Prescribing of antipyretics is illogical. A high fever of a meningitis patient is almost certainly due to that disease. If the remedy prescribed is effective in combating the organism reponsible for the meningitis, the temperature will subside. No additional drug is required to lower the temperature.

For many years the dangers of intracranial pressure were continually emphasized. In respect to such occurrences some have altered their views very little and feel that frequent lumbar punctures for drainage are needed. Nevertheless such practices were discontinued nearly 20 years[11] ago for my patients at County Hospital. Nor should it be necessary to withdraw cerebrospinal fluid at intervals in order to have a laboratory technician inform the physician whether his patient is gaining or losing ground in the battle for recovery. Another purpose for making lumbar punctures may be to determine the level in the spinal fluid of the drug which is being administered. But a satisfactory estimation can be made by obtaining a blood level which usually exceeds the spinal fluid level by 25 to 50 per cent. However, the concentration of the drug in cerebrospinal fluid about the brain cells may not be the same as in the lumbar region. Therefore it may be argued that withdrawal of spinal fluid by lumbar puncture to determine drug levels can not be true indications of concentrations in the cerebrospinal fluid throughout its circulation, and consequently are of little value.

Most of the deaths attributable to meningococcic infections are due to the Waterhouse-Friderichsen syndrome in which there are massive hemorrhages in the adrenal glands. Shock is the predominating symptom that calls for treatment, but although recoveries have been reported, a fatal termination is usual and may occur within a few hours after onset of the illness. If life is prolonged, cortisone may be given in 25 milligram doses 3 to 4 times daily, and is believed to be of value. For many years we used cortical extract which never impressed me as being helpful. Artificial

respiration may be necessary and blood transfusions an aid in addition to terramycin or aureomycin, intravenously. It is also well to place the patient in an oxygen tent, but survival is extremely doubtful.

H. influenzae meningitis can be cured with aureomycin, terramycin or chloromycetin. In a single instance, where achromycin was the remedy, a remarkable recovery occurred in one of our patients. Although good results have been obtained with streptomycin[15] there is no need of using that drug now. Streptomycin and dihydrostreptomycin should be avoided, especially for infants and young children, if it is possible to do so. If from the use of those drugs there is loss of hearing in an infant, the child may grow up as a deaf mute.

For pneumococcic meningitis we have had good results with penicillin, terramycin and aureomycin. If penicillin is selected, massive doses are required but if desired all can be given by the intramuscular route. Usually sulfadiazine or gantrasin is given in combination if penicillin is used. When the diagnostic lumbar puncture is made, the cerebrospinal fluid examination often seems to be of value for prognosis. If there is a high cell count, but few organisms found on smear, the outcome should be favorable, but if the cell count is low, less than a thousand, and diplococci very numerous, the prognosis is not good. These signs seem fairly dependable, regardless of the patient's age.

In the past some excellent results were reported with the use of sulfonamides and penicillin in combination for treatment of pneumococcic meningitis in infants under one year of age. Penicillin was given intrathecally and that route was considered to be of great importance. But the length of time required for recovery seems to be much less without intrathecal therapy when some of the newer antibiotics are prescribed. However, no one should expect any kind of meningitis to be subdued completely within 3 to 4 days. But there always seems to be an urge to use the needle. At present, the younger physicians, in particular, are likely to feel that if an infant with meningitis has a temperature above normal after 7 days treatment that there must be a subdural effusion and a puncture made to test that possibility. It is my opinion that the dangers from subdural effusions are magnified and that too many exploratory punctures are being made.

Tuberculous meningitis manifests greater resistance to treatment than any of the ordinary forms of meningeal infections. Nevertheless it is often surprising to see what can be accomplished with prolonged therapy. Some of our best results have been brought about by intramuscular streptomycin as the sole remedy. Even

MENINGITIS IN CHILDREN

| | WHITE | NEGRO | MALE | FEMALE | TOTAL |
|---|---|---|---|---|---|
| **MENINGOCOCCIC** | | | | | |
| Under 1 YR | 9 | 5 | 8 | 6 | 14 |
| 1-5 | 23 | 19 | 26 | 16 | 42 |
| 5-10 | 2 | 8 | 6 | 4 | 10 |
| 10-15 | 4 | 2 | 5 | 1 | 6 |
| TOTAL | 38 | 34 | 45 | 27 | 72 |
| **H INFLUENZAE** | | | | | |
| Under 1 YR | 1 | | | 1 | 1 |
| 1-5 | 1 | 1 | | 2 | 2 |
| 5-10 | | | | | 0 |
| 10-15 | 1 | | 1 | | 1 |
| TOTAL | 3 | 1 | 1 | 3 | 4 |
| **PNEUMOCOCCIC** | | | | | |
| Under 1 YR | | 1 | | 1 | 1 |
| 1-5 | 1 | 2 | 2 | 1 | 3 |
| 5-10 | 1 | | 1 | | 1 |
| 10-15 | 1 | 1 | 2 | | 2 |
| TOTAL | 3 | 4 | 5 | 2 | 7 |
| **TUBERCULOUS** | | | | | |
| Under 1 YR | | 1 | | 1 | 1 |
| 1-5 | 1 | 2 | 1 | 1 (D) | 2 |
| 5-10 | 2 | 2 | 4(1D) | 1 | 5 |
| 10-15 | | 2(1D) | 2 | | 2 |
| TOTAL | 3 | 7 | 7 | 3 | 10 |
| GRAND TOTAL | 47 | 46 | 58 | 35 | 93 |

patients with a miliary tuberculosis have recovered—not merely "survived" as is sometimes said. But improvement is slow and 3 to 4 months of therapy have been necessary. After that time isoniazid orally may be prescribed for an additional period depending on the patient's condition.

For a young child our dosage of streptomycin has varied from 0.5 gram to 1.0 gram daily. For older patients a dosage of 1 to 2 grams daily was used. Only on a few occasions was dihydrostrepto-

mycin given. More recently some of the patients have also received both paraminosalicylic acid and isoniazid, the dosage for the latter drugs being one dram t.i.d. and 25 milligrams t.i.d., respectively. In a few foreign countries both of these two drugs have been administered intravenously and isoniazid also prescribed intrathecally. From time to time in the course of treatment a blood transfusion is beneficial if a patient does not respond rapidly.

The prognosis for the colored race is considered less favorable than for the white with tuberculous meningitis. Nevertheless, most of our patients have been negroes. Yet it seems to be true that a white patient responds to treatment more rapidly.

Many innovations have been tried for the treatment of tuberculous meningitis, including burrows in the skull for introduction of remedies and injecting tuberculin intraspinally. However, we feel that the methods I have briefly described are fairly satisfactory.

Sometimes the statement is made that every meningitis patient has encephalitis. It has also been asserted that sequellae affecting the mental faculties are more frequent since the introduction of modern drugs than formerly. Among the patients who have come under my observation there has been no evidence produced to substantiate either of those beliefs.

## COMMENT

Clinical signs of meningitis in infants are not always apparent. In older children, certain characteristics can be observed sometimes which point to the bacteriologic diagnosis. A lumbar puncture should be required only when it is necessary for a bacteriologic diagnosis which can not be determined without examination of the cerebrospinal fluid.

Intrathecal therapy is not needed[16] for the successful treatment of any kind of meningitis. With intrathecal therapy complications[17] are more numerous.

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TOXOPLASMOSIS IN RELATION TO MENTAL DEFICIENCY. (British Medical Journal, London, 1: 702, March 28, 1953). Of 698 mentally deficient patients, most of them children, 55 showed positive toxoplasmin skin and dye reactions. The incidence of positive reactions increased with advancing age. The 55 positively reacting patients were examined physically, ophthalmoscopically, and radiologically for signs of toxoplasmosis. The criteria cited by Sabin in 1948 served as a guide. They include internal hydrocephalus or microcephaly, chorioretinitis with predilection for the macular rgion, convulsions and other signs of involvement of the nervous system, and cerebral calcification. In two cases eye lesions suggestive of toxoplasmosis were found. Radiologic examination and lumbar puncture showed nothing suggestive of toxoplasmosis. In none of the cases could the mental defect be definitely attributed to toxoplasmosis. In some cases other causal factors were present, for example, epiloia (tuberous sclerosis), phenylketonuria, or mongolism. It was concluded that in mental institutions or elsewhere a positive toxoplasmin reaction is acquired like a positive Schick reaction with increasing age and is very infrequently associated with clinical toxoplasmosis, and that toxoplasmosis is not a common cause of mental defect.—*Journal A.M.A.*

# PEDIATRICS AT THE TURN OF THE CENTURY

*From time to time the Archives, which was the first Children's Journal in the English language, will reprint contributions by the pioneers of the specialty over fifty years ago. It is believed that our readers will be interested in reviewing such early pediatric thought.*

## PRIMARY ADENOSARCOMA OF THE LIVER*

### Report of Case in a Child of Nine Months

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New York.

The patient was a male child admitted to the Babies' Hospital April 4, 1904, on account of an abdominal tumor.

The parents were both living and healthy, also one other child; there was a history of tuberculosis in the father's family, but nothing else which bore even remotely upon the case could be ascertained. The patient was born at term after an easy labor, had been breast-fed and was reported always to have been a pale child but well nourished and had gained steadily in weight. The child did well up to the age of seven months when, on account of some digestive disturbance, chiefly vomiting, bottle-feeding was substituted for part of the nursings. The vomiting had recurred at varying intervals until the patient was admitted. The stools were green and undigested and the child lost weight, though not rapidly. The only symptoms noticed had been this disturbance of digestion until the week before admission, when a tumor of the abdomen was discovered on account of which the child was sent to the hospital.

The examination on admission showed a well developed but pale and rather poorly nourished child; weight 15¼ pounds; four teeth; nothing abnormal in heart or lungs. The abdomen was moderately distended, being distinctly more prominent on the right side than on the left. Here was felt a large tumor forming a hard mass extending, at the ensiform cartilage, about two inches to the left of the median line; at the umbilicus, a little to the left of the median line. Its lower border extended in a curved direction from just below the umbilicus to the crest of the ilium.

*Read before the Sixteenth Annual Meeting of the American Pediatric Society, Detroit, Mich., June 1, 1904.
Reprinted from Archives of Pediatrics, 22: 248-256, April 1905.

Its surface was smooth and semi-elastic. Continuous flatness on percussion extended from the sixth rib to the lower border of the tumor. A mass was felt in the left side of the abdomen corresponding to the spleen. Neither by palpation or percussion could the liver be made out as separate from the tumor. The skin over the abdomen was normal except for a slight distension of the superficial veins. No other masses could be felt in the abdomen or in the pelvis; genitals normal. There was slight edema of both feet and legs; no paralysis. There were no nodular enlargements except slight ones in the cervical region. The examination of the blood showed hemoglobin, 55 per cent.; leukocytes, 17,000; fresh blood, normal.

An exploratory needle was passed into tumor about its middle and 2 cc. of bloody fluid withdrawn. The microscopical examination showed, red blood cells, fatty liver cells, fat droplets and small round mononuclear cells. Culture sterile.

After the child had been under observation for three days, as it was growing steadily worse, exploratory incision was decided upon. Up to this time slight fever had been present, 100°-101°F., and occasionally vomiting, but there was no jaundice; no absence of bile from the stools was noticed. The child looked very sick; took food very badly.

The operation was performed by Dr. A. L. Fisk under cocain anesthesia. A transverse incision was made about two inches below the costal margin over the most prominent part of the tumor. The tumor was found to be, as had been suspected, an enlarged liver, surface smooth and glistening. The liver was aspirated in various directions, but no pus found; but at one point, which seemed softer than the rest, an opening was made and a drainage tube inserted into the substance of the organ. This passed into a cavity apparently made up of broken down liver tissue as from it a grumous material was discharged, but no pus.

Considerable shock followed, but on the whole child bore it very well. After the operation the child lived thirteen days with a continuous but irregular temperature, steadily increasing prostration and gradual though not rapid loss in weight. Five days after the operation the leukocytes were 13,000. There were no local symptoms of importance; the wound was dressed daily and did well. The tumor did not change essentially in appearance.

There was occasionally vomiting but no diarrhea and little abdominal distension. The liver seemed slightly smaller during the last few days. Death occurred from exhaustion.

PATHOLOGICAL REPORT

Autopsy, twelve hours after death. Body, well nourished; edema of feet and hands; operation wound 4 cm. long to the right and above the umbilicus. Wound normal.

*Liver.* Measures 19 cm. long, 21 cm. wide, 10 cm. thick; weight, 735 grams; of a light brown color, anterior surface mottled, with lighter and darker areas. There was a rounded, bulging and apparently fluctuating mass measuring 9 x 7 cm., which projected somewhat above the level of the rest of the organ. This extended nearly to the lower border of the liver. The lower border of the liver is sharp not rounded. The operation wound, 2 cm. long, penetrates the softened prominent tumor mass at its centre. The anterior part of this protruding tumor fluctuates, but this is due to necrosis; the rest of the tumor, exposed by section of the liver, is a firm, nodular, yellowish-white color mottled with larger and smaller hemorrhagic areas and separated from the liver substance by thin capsule. The softened portions are limited to the anterior part. In the interior there are found only a few scattered softened nodules, some of which are black in color from hemorrhage. The liver substance outside the growth is firm and moderately fatty. The posterior surface of the liver shows a mottling due to the presence of the tumor. Near its upper border are three small separated yellow nodules. The liver capsule is smooth, there is no peritonitis and apparently no thickening of the interlobular connective tissue septa. Gall bladder 4 cm. long contains fluid bile; ducts are all pervious.

There was a slight recent pericarditis and a moderate bronchopneumonia. All the other viscera were essentially normal, except the kidneys, which showed slight recent nephritis, no metastasis being present anywhere.

Cultures from the heart, liver, spleen and kidneys gave a pure growth of the streptococcus pyogenes. This was evidently a terminal infection.

*Microscopical Examination.* In sections from the periphery of the tumor, the capsule is seen to be composed of a layer of cirrhotic

liver substance in which newly-formed bile ducts are found in small numbers. The growth is made up of lobules of liver cells, arranged in atypical columns; the central vein is often at one side of the lobule, and again it cannot be found. Small interlobular blood capillaries are numerous, and many small hemorrhages have taken place in and between the lobules. The epithelial cells show many karyokinetic figures.

Sections from the softened hemorrhagic portion near operation wound showed two varieties of cells. The epithelial cells resembling those of the liver are arranged in the adenomatous lobules as in the rest of the tumor. In addition there are irregular, larger and smaller masses of round cells whose nuclei stain deeply and are comparatively large. These cells lie in a very delicate stroma of connective tissue fibrils. Small blood vessels are very numerous, and hemorrhages into the tissue have taken place. The softened areas seen in the gross specimen are due to large hemorrhages in this portion of the growth which is evidently a small round cell sarcoma. The sarcoma nodules lie between the adenomatous ones and in places they grow into the latter, i.e., between the columns of epithelial cells are irregularly-sized sarcoma nodules. At the capsule the sarcoma cells infiltrate the connective tissue for some distance in contrast to the adenoma which is sharply limited.

The liver substance outside the tumor maintains its lobular structure perfectly. The liver cells contain smaller and larger fat droplets, especially at the periphery of the lobules. The connective tissue septa are not thickened—there is no general cirrhosis.

*Remarks.* No exactly similar case can be discovered in medical literature. But two liver adenomata in children have been found recorded: one aged twenty months in which Weichselbaum made the microscopic examination, and the other in a boy of twelve years, described by Pye-Smith.

The case here reported would come under the head of the *hepato adenoma proprium* of Witwicky, the cells of the neoplasm originating from those of the liver, as distinct from the epithelium of the bile ducts, and being arranged in columns. Such growths do not become malignant and form no metastases.

Primary congenital sarcomata of the liver have been described by Pepper in an infant eight weeks old; by Heaton at the same age; by Parker in a baby of three weeks, Pepper at seven weeks,

Gee at five months and by De Ruyter. All of these were round-celled sarcomata. Meisenbach's case, four months old, was a myxosarcoma. Windrath describes a spindle-cell sarcoma in a baby less than one year old. Bauman and Forbes' case eleven months old, was a round and spindle-celled sarcoma. West's case, eight months old, was a medullary sarcoma. Henoch gives no microscopic details of the sarcoma he reports in a child of two and a half years. Roberts reports a medullary sarcoma in a girl twelve years old. Several of these cases were accompanied by metastases in the suprarenal capsules and in the lung. In addition to these primary cases quite a large number of secondary sarcomata in the liver in children have been reported.

The combination of adenoma and sarcoma would seem to be unusual among the tumors of the liver occurring in infants. The presence of a distinct capsule around the whole neoplasm, and, the fact that the sarcoma is not found in all parts but only in the central zone, would seem to argue that the adenoma was the original process, to which the sarcoma was added at a somewhat later date.

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FATAL GENERALIZED VACCINIA. (Archives of Disease in Childhood, London, 28:110, April 1953). A fatal case of generalized vaccinia is reported in an 11-week-old baby girl. Secondary lesions developed around the vulva and the anus and on the dorsum of the left hand two weeks after vaccination against smallpox, and widespread cutaneous lesions appeared on the right hand and the face until death occurred five weeks later. In the course of a normal vaccination, virus-neutralizing antibodies appear in the blood at about 12 to 14 days and continue to rise until about the 21st day, when they attain a steady level. Such neutralizing antibodies failed to develop in the serum of the authors' patient and electrophoretic analysis showed complete absence of gamma globulin. Treatment with penicillin and aureomycin was ineffective, as were transfusions of blood from recently vaccinated donors and intramuscular administration of 750 mg. of gamma globulin. It would seem that hyperimmune animal serums or convalescent serum from a recent case of smallpox should be given in large doses at frequent intervals. The possibility of replacement transfusions should be considered if serum is not available.—*Journal A.M.A.*

# DEPARTMENT OF ABSTRACTS

JOHNSON, A. M. AND SZUREK, S. A.: ETIOLOGY OF ANTISOCIAL BEHAVIOR IN DELINQUENTS AND PSYCHOPATHS. (Journal American Medical Association, 154:814, March 6, 1954).

We have assimilated material from more than a decade of research and collaboration dealing with the cause of antisocial behavior in "good" families. The same cause is involved in the delinquent and in the psychopath, who is just a delinquent grown older. Of course, the more private family delinquencies in some instances may overlap the sociologic or gang antisocial behavior. By means of simultaneous psycho-therapy of the parents and the child, we observed that the parents unwittingly condone and foster the child's living out the parents' own poorly inhibited antisocial impulses, so that the parents may achieve vicarious gratification. This obtains for stealing, recurrent fire-setting, sexual destructiveness, vandalism and serious recurrent criminal behavior. A defect in conscience is permitted to develop in the child by the parents so that the parents unconsciously can achieve pleasure by permitting the child to misbehave seriously. The frequent parental hostile destructiveness toward the child who is the scapegoat and the unique significance of the choice of this particular child as scapegoat always can be discovered by thorough study of the parents. A multiplicity of variables of mixed quality and quantity enters into the family rearing of any child, but the specific stimulus for the actual living out of a child's antisocial behavior is the unconscious, less often conscious, sanction from the parent. This specific behavior of the child is traceable to a specific defect in the parents' own conscience or integration in this area of behavior. It is advocated that there be a disseminated knowledge of these origins of delinquency, aimed at the erection of parental conscience barriers against the fostering of vicarious misbehavior, since such behavior may be transmitted from generation to generation through interpersonal living. Individual neuroses that may result, regardless of their severity, are more amenable to treatment than is the delinquency complex.

AUTHORS' SUMMARY.

HELLSTROM, B. AND JONSSON, B.: LATE PROGNOSIS IN ASPHYXIA NEONATORUM. (Acta Paediatrica 42:398, Sept. 1953).

Eighty-five children treated at a children's hospital for asphyxia neonatorum were subjected to a follow-up examination. Eighteen died during the newborn period. Sixty-five of the 67 survivals were followed up. Among them 18 showed signs of a permanent cerebral injury (spasticity, mental retardation, convulsions). The late prognosis was correlated to different clinical symptoms during the newborn period. Children with convulsions, changed tonus, bulging fontanel, reduced sucking capacity have a conspicuously bad prognosis. AUTHORS' SUMMARY.

BICKEL, H.; GERRARD, J. AND HICKMANS, E. M.: THE INFLUENCE OF PHENYLALANINE INTAKE ON THE CHEMISTRY AND BEHAVIOUR OF A PHENYLKETONURIC CHILD. (Acta Paediatrica, 43:64, Jan. 1954).

Phenylketonuria is a not uncommon cause of mental deficiency (there are probably 1600 cases in Great Britain alone). On the supposition that the high level of phenylalanine or its breakdown products in the blood and cerebrospinal fluid might be responsible for the mental retardation in this disorder, we have treated a two-year-old child with a diet low in phenylalanine. The introduction of this diet was associated with an appreciable improvement in the patient's mental status and a fall in the level of phenylalanine in the blood and urine. When phenylalanine was again given in fairly large amounts, there was an immediate and dramatic deterioration in the child's mental and biochemical condition. A similar phenylalanine intake produced no clinical reaction in a control child. The main source of aminoacids in the diet was an acid casein hydrolysate which was specially created to remove phenylalanine. The aim of the phenylalanine-poor diet was to keep the phenylalanine blood level as near the normal range as possible. The preparation of such a diet presents little difficulty, if a phenylalanine-free casein hydrolysate is available. Its value in the treatment of other children is at present being investigated; it seems reasonable to assume that patients in the first 2 years of life will benefit most.

AUTHORS' SUMMARY.

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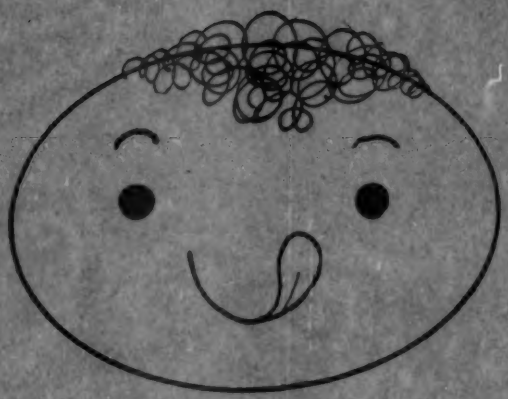

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*Lawler, E. G. et al.: Clin. Med. 61:207 (March) 1954.

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